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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/802,110	03/07/2001	James Leushner	VGEN.P-058-2	5580

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EXAMINER	
WILDER, CYNTHIA B	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 11/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/802,110	LEUSHNER ET AL.	
	Examiner	Art Unit	
	Cynthia B. Wilder, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,17-25 and 29-36* is/are rejected.

7)☒ Claim(s) *14-16, 26-28* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

FINAL ACTION

1. Finality as set forth in the previous Office action is withdrawn and prosecution is reopened to address new grounds of rejections made in the previous Office action. Accordingly, this Office action is now made FINAL. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Previous Rejections

3. The prior art rejection under 35 USC 102(e) as being anticipated by Jordon et al is withdrawn in view of Applicant's arguments. The prior art rejection under 35 USC 103(a) is maintained and discussed below.

Claim Rejections - 35 USC § 103

4. Once again, claims 13, 17-25 and 29-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mathies et al (Us 5,707,804, filing date March 1995) and Ruano (5,427,911, (patent date June 27, 1995) in view of Rao (Analytical Biochemistry, vol. 216, pages 1-14, (1994) and further in view of Ahern (The Scientist, Vol. 9, No. 15, pages 1-15, June 1995). Regarding claims 13, 17-25 and 29-36, Mathies et al teach a method and kit for sequencing nucleic acid, the method comprising primer pairs for copying a single stranded nucleic acid and dideoxynucleotide for terminating the chain at a particular nucleotide, the mixture further comprising a DNA polymerase, dNTPS and separate reaction vessels to generate the single stranded DNA fragments (col. 10, lines 26-62 and col. 14, lines 12-26). Mathies do not teach wherein all of the sequencing reagents are in the form of a kit.

Ruano et al. teach a method for sequencing genomic DNA sample, the method comprising amplifying in vitro with two locus specific primers that flank both ends of the target region to obtain a template, synthesizing simultaneously truncated strands from both ends of the template by introducing a dideoxynucleotide terminator for each of the four bases adenine, guanine, cytosine and thymine and introducing a label or labels specific for either or both of the 5' ends of the synthesizing strands, thermally cycling steps to provide a sufficiently readable signal (col. 2, lines 3-23). Ruano further teaches wherein the dideoxynucleotide triphosphate is in a mole ratio of about 1:10 to the corresponding deoxynucleotide triphosphate (col. 6, lines 47-68).

The reference of Ruano differs from the instant invention in that the reference does not teach wherein the method comprises the dideoxynucleotide triphosphate in a mole ratio of 1:50 to 1: 1000 or in a mole ratio of 1:1000 to 1: 500 to the corresponding deoxynucleotide triphosphates.

In a method similar to that of Ruano, Rao teaches a method of direct sequencing of polymerase chain reaction-amplified DNA. Rao teaches wherein the method comprises mixing the PCR-amplified genomic DNA, labeled primer sequencing buffer and Taq polymerase in a tube, adding to the mixture in four separate tubes, four dNTPs and at least one dideoxynucleotide triphosphate, perform thermal cycling (see Table 3, page 5). Rao differs from the instant invention in that Rao does not teach wherein the mole ratio of the ddNTP:dNTP is from 1:50 to 1:1000 or 1:100 to 1:500. Rao also does not teach wherein the polymerase enzyme incorporates dNTPs into an extending nucleic acid polymerase at a rate which is no less than 0.5 times the rate of incorporation of dNTPs. However, Rao discloses that the composition of the

dNTP/ddNTP mix varies depending on the type of polymerase preparation used. Rao additionally states that different polymerases require different dNTP/ddNTP ratios for optimal chain terminations and therefore, the reagents or kits for one polymerase cannot be substituted with those for a different polymerase. Rao further teaches that optimal buffer conditions for the synthesizing reaction will vary based on the specific DNA polymerase used (see Table 3 legend).

In a review article Ahern teaches the advantages of a kit. Ahern teaches that a kit provides convenience, time management and ease of practicing to the investigator (page 4, second-forth paragraphs). Therefore in view of the foregoing, one of ordinary skill in the art at the time of the claimed invention would have recognized that the mole ratio of reagents of the kit and polymerase extending ability would vary based on the choice of polymerase preparation used in the sequencing reaction and desired results as suggested by Rao. One of ordinary skill in the art at the time of the claimed invention would have been further motivated to have combined the components of the sequencing method as taught by Ruano and Rao in the form of a kit for the obvious benefits taught by Ahern that a kit provides convenience, time management and ease of practicing to the investigator.

Applicant's traversal

5. Applicant traverses the rejection on the following ground: Applicant summarizes MPEP 706.02 and states that the examiner has not explained how the cited references teach or suggest all the claimed limitations. Applicant states that as noted above, the Examiner previously withdrew 103(a) obviousness rejections based on the Ruano, Rao, and Ahern references. Applicant states that Rao teaches use of radiolabeled primers that must be separated in different

reaction vessels, that Ruano teaches a plurality of reaction vessels and fails to teach that the reagents for both sense and antisense strands are mixed in the same reaction vessel and that Ahern merely describes the general concept of a kit, without and details pertinent to the claimed invention. Applicant states that the Examiner agreed with the above arguments, and withdrew the rejection. Applicant states that the Examiner has not raised any additional arguments in respect of these references and has not provided Applicant with any explanations why these references, which the Examiner previously agreed did not teach or suggest the elements of the present invention, now render the claimed invention obvious. Applicant states that the Examiner has officially acknowledged that prior art does not render the claims obvious and then elects to reverse that determination. Applicant states that the Applicant is entitled to a detailed explanation of the reasons for doing so. Applicant argues that the Examiner now reasserts these references Ruano, Rao and Ahern in the current rejection combined with the additional reference of Mathies. Applicant argues that with respect to Mathies, Applicant reiterates the rejection and states that Mathies teaches primers for copying a single stranded nucleic acid. Applicant states that Mathies thus fails to teach reagents in a single reaction vessel capable of sequencing both sense strands of genomic DNA. Applicant states that neither do any of the secondary references compensate for or provide any teaching or suggesting of this element of the claimed invention. Applicant states indeed, not a single one of theses references teach the limitations of a single reaction vessels containing a mixture of reagents capable of sequencing both the sense and antisense strands of a DNA template. Applicant concludes that for theses reasons, the combination of references recited in the previous Office action teach or suggest the present invention. Applicant respectfully request the rejection be withdraw and claims allowed.

Examiner's Response

6. All of the arguments have been thoroughly reviewed and considered but are not found persuasive for the reasons that follow: In regards to Applicant's arguments that the Examiner previously withdrew 103(a) obviousness based on the Ruano, Rao and Ahern references and now reinstated them, it is noted that the new grounds of rejections introduced in the previous Office action were necessitated by Applicant's amendment of the claims. MPEP 714.04 states that "if the claims as amended are clearly open to rejection on grounds of record, a final rejection should generally be made." Further contrary to Applicant's arguments, the rejection under 35 US 103(a) made in the previous Final office action was not made over Ruano, Rao and Ahern, but rather was made over Mathies in view of Ruano, Rao and Ahern. The combination of Ruano in view of Rao and Ahern was previously withdrawn based on previous amendments made to the claims and not the claims as currently amended. Likewise, the secondary references of Ruano, Rao and Ahern are currently cited for the teachings not found in the primary reference of Mathies necessitated by Applicant's amendment.

In regards to Applicant's arguments that the primary reference of Mathies does not teach the claimed invention because the reference of Mathies teaches primers for copying a single stranded nucleic acid, it is noted that the claims as broadly written are repleted with intended use limitations. The claims are drawn to a product and not a method. The claims do not recite any structural properties or features of the claimed product which distinguishes it over the prior art. For example, such limitations as "for each DNA region to be sequence" and "for sequencing sense and antisense strands" are intended use limitations of the claimed reagents in the product

and does not provide any structural features for the claimed reagents. MPEP states "a recitation of an intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

MPEP further states that "language that suggests or makes optional but does not require steps to be performed or does not limit a claim to a particular structure does not limit the scope of a claim or claim limitation". In this case, the claims as broadly written only require "a kit comprising a single reaction vessel containing a mixture of region specific sequencing reagents, wherein said region-specific reagents comprises region-specific primers.

The primary reference of Mathies meets this limitation in the teaching of region specific primers in a single reaction vessel in the form of a kit. Mathies teach that theses reagents are used in a sequencing reaction. Mathies also meets some of the optional limitations recited in the claims. However, it is noted that these features are not required as the claims recite that they are *"optional"*. The secondary references of Ruano, Rao and Ahern are cited to meet the limitations of the additional features recited in the dependent claims recited therein. For example, the secondary reference of Ruano et al teach a method and region specific reagents comprising locus specific primers that flank one or more DNA region within genomic DNA. Like Mathies, Ruano also teaches that the reagents are used in a sequencing reaction. The tertiary reference of Rao likewise is also used in sequencing reactions and is included in the obviousness rejection for its teaching of reagents recited in the dependents claims and not found in the primary reference of Mathies and secondary reference of Ruano et al. Finally, the

reference of Ahern is cited to strengthen motivation for wanting to combine the reagents used in the various sequencing reactions in the form of a kit. The combination of the references meets the limitations of the rejected claims recited above. Applicant's arguments are not sufficient to overcome the prior art rejections made under 35 USC 103(a). Accordingly, the rejections are maintained.

Conclusion

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-0791. The examiner works a flexible schedule and can be reached by phone and voice mail. Alternatively, a request for a return telephone call may be emailed to cynthia.wilder@uspto.gov. Since email communications may not be secure, it is suggested that information in such request be limited to name, phone number, and the best time to return the call.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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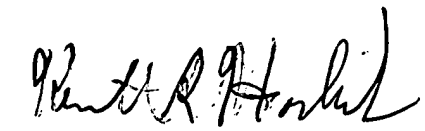

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER

11/28/05